AMENDMENTS TO THE CLAIMS

1. (original): A method for counteracting a pathologic change in the β-adrenergic signal transduction pathway, comprising administering to a mammalian subject in need an effective amount of a compound capable of inhibiting TGF-β signaling through a TGF-β receptor

2. (original): The method of claim 1 wherein the TGF-β receptor is a TGFβ-R1 receptor kinase.

3. (original): The method of claim 2 wherein said compound is capable of specific binding to a TGFβ-R1 receptor kinase.

4. (original): The method of claim 2 wherein said compounds preferentially inhibits a biological activity mediated by a TGFβ-R1 receptor kinase.

5. (original): The method of claim 1 wherein the pathologic change is selected from the group consisting of (a) a reduction in the mRNA level of a β-adrenergic receptor, (b) a reduction in the number of β-adrenergic receptor binding sites, (c) TGF-β-induced down-regulation of Smad3 expression, and (d) loss in β-adrenergic sensitivity.

6. (original): The method of claim 5 wherein the loss in β-adrenergic sensitivity is associated with the administration of a β-adrenergic agonist.

7. (original): The method of claim 6 wherein the loss in β-adrenergic sensitivity results from long-term or excessive administration of a β-adrenergic agonist.

8. (original): The method of claim 7 wherein the β-adrenergic agonist is selected from the group consisting of procaterol, albuterol, salmeterol, formoterol, and doputamine.

9. (original): The method of claim 1 wherein the pathologic change is observed in lung tissue.

10. (original): The method of claim 9 wherein the pathologic change results in a disease or condition benefiting from the improvement of lung function.

11. (original): The method of claim 10 wherein the disease or condition is a bronchoconstrictive disease.

12. (original): The method of claim 10 wherein the disease or condition is selected from the group consisting of emphysema, chronic bronchitis, chronic obstructive pulmonary disease (COPD), pulmonary edema, cystic fibrosis (CF), occlusive lung disease, acute respiratory deficiency syndrome (ARDS), asthma, radiation-induced injury of the lung, and lung injuries resulting from other factors, such as, infectious causes, inhaled toxins, or circulating exogenous toxins, aging and genetic predisposition to impaired lung function.

13. (original): The method of claim 12 wherein the mammalian subject is human.

14. (original): The method of claim 13 wherein the human subject is in need of bronchodilation.

15. (original): The method of claim 1 wherein the pathologic change is observed in cardiac tissue.

16. (original): The method of claim 15 wherein the mammalian subject is human.

17. (original): The method of claim 16 wherein the human subject has been diagnosed with a heart disease.

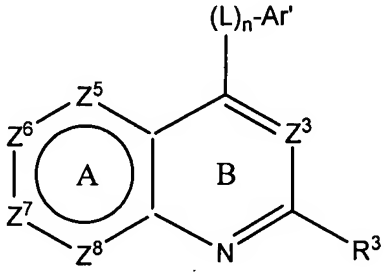
18. (original): The method of claim 17 wherein the heart disease is chronic or congestive heart failure (CHF).

19. (original): The method of claim 3 wherein the compound is capable of binding to an additional receptor kinase.

20. (original): The method of claim 19 wherein the additional receptor kinase is an activin receptor (Alk4).

21. (original): The method of claim 2 wherein the compound is a small organic molecule.

22. (original): The method of claim 21 wherein the small organic molecule is a compound of formula (1)



(1)

or the pharmaceutically acceptable salts thereof

wherein R^3 is a noninterfering substituent;

each Z is CR^2 or N, wherein no more than two Z positions in ring A are N, and

wherein two adjacent Z positions in ring A cannot be N;

each R^2 is independently a noninterfering substituent;

L is a linker;

n is 0 or 1; and

Ar' is the residue of a cyclic aliphatic, cyclic heteroaliphatic, aromatic or heteroaromatic moiety optionally substituted with 1-3 noninterfering substituents.

23. (original): The method of claim 22 wherein the compound is a quinazoline derivative.

24. (currently amended): The method of claim 23 wherein ~~wherein~~ Z^3 is N; and Z^5-Z^8 are CR^2.

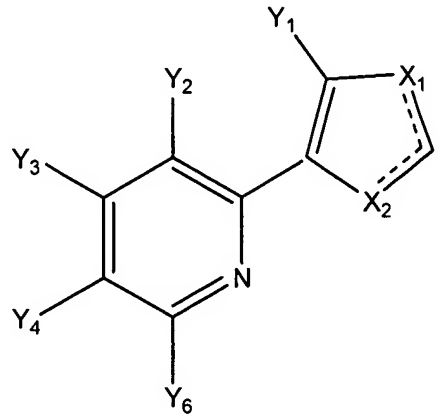
25. (original): The method of claim 23 wherein Z^3 is N; and at least one of Z^5-Z^8 is nitrogen.

26. (original): The method of claim 23 wherein R^3 is an optionally substituted phenyl moiety

27. (original): The method of claim 26 wherein R^3 is selected from the group consisting of 2-, 4-, 5-, 2,4- and 2,5-substituted phenyl moieties.

28. (original): The method of claim 27 wherein at least one substituent of the phenyl moiety is an alkyl(1-6C), or halo.

29. (currently amended): The method of claim 21, wherein the small organic molecule is a compound of formula (2)



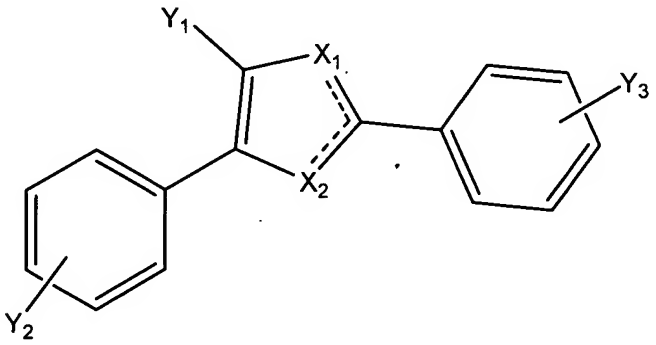
wherein Y_1 is phenyl or naphthyl optionally substituted with one or more substituents selected from halo, alkoxy(1-6C), alkylthio(1-6C), alkyl(1-6C), haloalkyl (1-6C), -O-$(CH_2)_m$-Ph,

-S-$(CH_2)_m$ -Ph, cyano, phenyl, and CO_2R, wherein R is hydrogen or alkyl(1-6C), and m is 0-3; or phenyl fused with a 5- or 7-membered aromatic or non-aromatic ring wherein said ring contains up to three heteroatoms, independently selected from N, O, and

Y_2, Y_3, Y_4, and Y_5 independently represent hydrogen, alkyl(1-6C), alkoxy(1-6C), haloalkyl(1-6C), halo, NH_2, NH-alkyl(1-6C), or $NH(CH_2)_n$-Ph wherein n is 0-3; or an adjacent pair of Y_2, Y_3, Y_4, and Y_5 form a fused 6-membered aromatic ring optionally containing up to 2 nitrogen atoms, said ring being optionally substituted by one or more substituents independently selected from alkyl(1-6C), alkoxy(a-6C), haloalkyl(1-6C), halo, NH_2, NH-alkyl(1-6C), or $NH(CH_2)_n$-Ph, wherein n is 0-3, and the remainder of Y_2, Y_3, Y_4, and Y_5 represent hydrogen, alkyl(1-6C), alkoxy(1-6C), haloalkyl(1-6C), halo, NH_2, NH-alkyl(1-6C), or $NH(CH_2)_n$-Ph wherein n is 0-3; and

one of X_1 and X_2 is N and the other is NR_6, wherein R_6 is hydrogen or alkyl(1-6C).

30. (original): The method of claim 21 wherein said small organic molecule is a compound of formula (3)



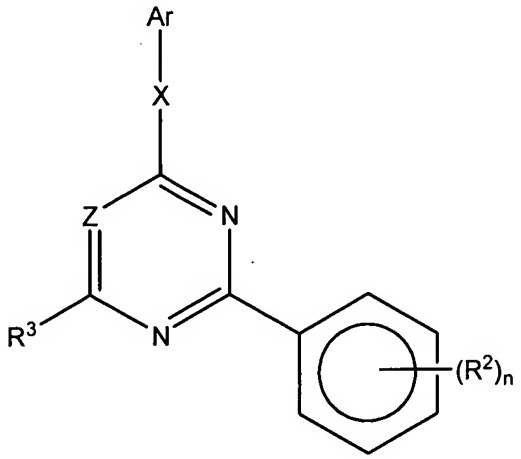
wherein Y_1 is naphthyl, anthracenyl, or phenyl optionally substituted with one or more substituents selected from the group consisting of halo, alkoxy(1-6C), alkylthio(1-6C), alkyl(1-6C), -O-(CH_2)-Ph, -S-$(CH_2)_n$-Ph, cyano, phenyl, and CO_2R, wherein R is hydrogen or alkyl(1-6C), and n is 0, 1, 2, or 3; or Y_1 represents phenyl fused with an aromatic or non-aromatic cyclic ring of 5-7 members wherein said cyclic ring optionally contains up to two heteroatoms, independently selected from N, O, and S;

Y_2 is H, $NH(CH_2)_n$-Ph or NH-alkyl(1-6C), wherein n is 0, 1, 2, or 3;

Y_3 is CO_2H, $CONH_2$, CN, NO_2, alkylthio(1-6C), -SO_2-alkyl(C1-6), alkoxy(C1-6), $SONH_2$, CONHOH, NH_2, CHO, CH_2NH_2, or CO_2R, wherein R is hydrogen or alkyl(1-6C); one of X_1 and X_2

is N or CR', and other is NR' or CHR' wherein R' is hydrogen, OH, alkyl(C-16), or cycloalkyl(C3-7); or when one of X_1 and X_2 is N or CR' then the other may be S or O.

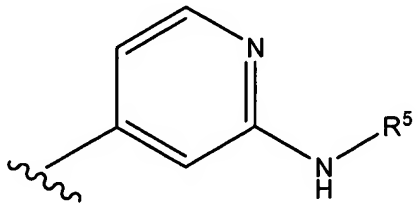
31. (original): The method of claim 21 wherein said small organic molecule is a compound of formula (4)



(4)

and the pharmaceutically acceptable salts and prodrug forms thereof; wherein

Ar represents an optionally substituted aromatic or optionally substituted heteroaromatic moiety containing 5-12 ring members wherein said heteroaromatic moiety contains one or more O, S, and/or N with a proviso that the optionally substituted Ar is not



wherein R^5 is H, alkyl (1-6C), alkenyl (2-6C), alkynyl (2-6C), an aromatic or heteroaromatic moiety containing 5-11 ring members;

X is NR^1, O, or S;

R^1 is H, alkyl (1-8C), alkenyl (2-8C), or alkynyl (2-8C);

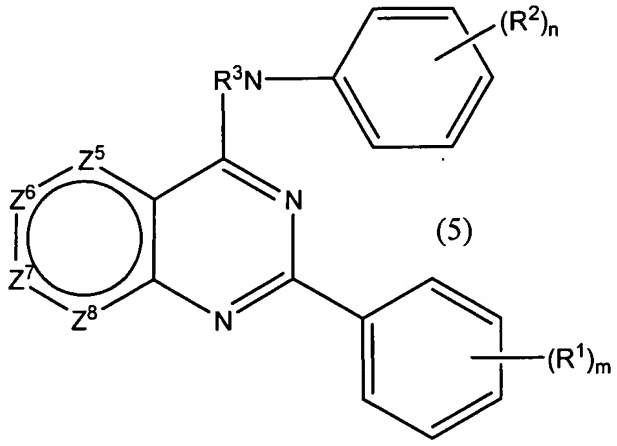
Z represents N or CR^4;

each of R^3 and R^4 is independently H, or a non-interfering substituent;

each R^2 is independently a non-interfering substituent; and

n is 0, 1, 2, 3, 4, or 5. In one embodiment, if n>2, and the R^2's are adjacent, they can be joined together to form a 5 to 7 membered non-aromatic, heteroaromatic, or aromatic ring containing 1 to 3 heteroatoms where each heteroatom can independently be O, N, or S.

32. (original): A method of claim 21 wherein said small organic molecule is a compound of formula (5)



(5)

or the pharmaceutically acceptable salts thereof;

wherein each of Z^5, Z^6, Z^7 and Z^8 is N or CH and wherein one or two Z^5, Z^6, Z^7 and Z^8 are N and wherein two adjacent Z positions cannot be N;

wherein m and n are each independently 0-3;

wherein two adjacent R^1 groups may be joined to form an aliphatic heterocyclic ring of 5-6 members;

wherein R^2 is a noninterfering substituent; and wherein R^3 is H or CH_3.

33-65. (canceled)